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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,196	11/20/2003	James R. Millis	3161-25-2	3652
22442	7590	07/30/2007		
SHERIDAN ROSS PC 1560 BROADWAY SUITE 1200 DENVER, CO 80202			EXAMINER WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	
			MAIL DATE	DELIVERY MODE
			07/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/719,196

Applicant(s)

MILLIS ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18,21-34 and 54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18, 21-34 and 54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Amendment filed September 13, 2006 is acknowledged. Claims 1-17 were previously canceled, claims 19, 20 and 35-53 have been currently cancelled; new claims 54 has been added. Claims 18, 24-28 have been amended. Currently pending claims 18, 21-34 and 54 reading on the elected invention are under examination.

Detailed Office Action

Rejections

Rejections made in Office Action of October 28, 2005 (previous action) and not repeated herein are moot or withdrawn, because the claims have been cancelled or amended, and applicants' arguments are found persuasive.

35 USC, section 112, second paragraph

Claim 18 is confusing as to the meaning of the phrase to «increase the action of the phosphatase having farnesyl pyrophosphate as a substrate». It is unclear what the phrase «to increase action of phosphatase» mean. The phrase is not defined by the claims or the specification. For examination purposes it is assumed that by increasing «action» of the enzyme applicants mean increasing its activity.

Claims 28 is rejected, because it is not known from which claim the claim depends.

Claim 34 depending on claim 31, and ultimately on claim 18, seeks to broaden the scope of claim 18. Claim 18 is directed to a method using a microorganism that is modified to decrease the action of the squalene synthase gene, thus by blocking the ergosterol pathway. However, the ergosterol pathway comprises 12 steps (according to Fig. 1) and blocking ergosterol pathway as broadly recited by claim 34 may take place by blocking steps other than synthesis of squalene by squalene synthase.

Claims 24-26 are confusing, because one skilled in the art who wants to produce farnesol would not transform a microorganism producing farnesol with geranylgeranyl pyrophosphate synthase. This would diminish the pool of farnesyl pyrophosphate available for production farnesol; see Fig. 1A-ii.

Claim 27 does not seem to further limit claim 18, which already recites the limitation « modified to increase the action [i.e. activity] of farnesyl pyrophosphate phosphatase ».

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Claim 54 is confusing as reciting *E. coli*, because *E. coli* does not possess any squalene synthase gene.

35 USC, section 112, first paragraph

Rejection for lack of written description

Claim 18, 21-34 and new claim 54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a genus of the methods for producing farnesol. The claims for a microorganism that is cultivated in a fermentation medium, has an isoprenoid metabolic pathway having and is modified to

- 1) decrease the action of the squalene synthase, and
- 2) to increase the action of phosphatase having farnesyl pyrophosphate as a substrate

The claims are lacking a sufficient written description of the claimed method, because they are lacking written description of a product which is used by said method. On page 19, paragraph 2.5 applicants teach about phosphatase modifications by stating,

"Both *S. cerevisiae* and *E. coli* contain numerous phosphatase activities. By testing several phosphatases for efficient dephosphorylation of FFP or GPP, one could select an appropriate phosphatase and express the gene encoding the enzyme in a production organism to enhance farnesol or GG production."

Applicants themselves have not performed said test, neither they used the gene encoding the phosphatase that is the most efficient in dephosphorylation of FPP. Applicants have not been in possession of a transformant engineered to express said phosphatase. Thus, what applicants are expecting from one having skills in the art is "a result that one might achieve if one made that

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invention"; see *Eli Lilly*, 119 F.3d at 1568. 43 USPQ2d at 1406 as quoted in MPEP page 2100-173 paragraph (2).

Claim 54 is rejected because *E. coli* produces FPP (page 132 of the specification line 5), but as such does not possess a squalene synthase gene, and the specification does not describe *E. coli* as a microorganism possessing a squalene synthase gene.

In conclusion, the subject matter of the claims is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejection for scope of enablement

Claims 18, 21-34 and new claim 54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *S.cerevisiae* engineered to decrease the action of the squalene synthase gene does not reasonably provide enablement for any microorganism engineered to increase the activity of the phosphatase specific for farnesyl pyrophosphate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of microorganism broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)); otherwise the experimentation left to those of skill in the art is undue.

The nature and breadth of the claimed invention encompasses the use of any gene encoding phosphatase specific for the FPP and genetic modification of any microorganism having an isoprenoid metabolic pathway to increase activity of said phosphatase. The specification does not provide any examples of such gene and modified microorganism, and a guidance is limited to:

"Both *S. cerevisiae* and *E. coli* contain numerous phosphatase activities. By testing several phosphatases for efficient dephosphorylation of FPP or GPP, one could select an

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appropriate phosphatase and express the gene encoding the enzyme in a production organism to enhance farnesol or GG production"; see page 19 of the specification.

In addition, to undue experimentation related to testing FPP phosphatases from *S. cerevisiae* and *E. coli* that are genetically well characterized, i.e., genes of the phosphatases produced by these microorganisms are known, the scope of the claims covers FPP phosphatases from any organism, thus FPP phosphatases that are unknown and encoded but genes thus far not cloned. Thus the experimentation left to those having skills in the art is not routine, improperly extensive and undue.

Double patenting*Statutory Double patenting*

Rejection of claim 24, as claiming the same invention as that of claim 24 of prior U.S. Patent No. 6,689,593 is withdrawn. In result of the current amendment the instant invention and invention of the patent are not patentably identical.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC)
at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner

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